```
HIV1-Vpr      1 M.....EQAP EDQGPQR.EY PNDWTLELLE ELKNEAVRHF PRIWLHSLGQ  44
HIV2/SIV-Vpr  1 M.....EERPP ENEGPQR.EP WDEWVVEVLE ELKEEALKHF DPRLLTALGN  45
HIV2/SIV-Vpx  1 MTNPRETIPP GNSGEETIEE AFDWLDRTVE AINREAVNHL PRELIFQVWQ  50

HIV-Vpr      45 HIYETYGDTW TGVEALIR.. ....ILQQLLF IHFRIGCRHS RIGIIQQRRT  89
HIV2/SIV-Vpr 46 HIYNRHGDTL EGAGELIR.. ....ILQRALF MHFRGGCIHS RIGQPGGGNP  90
HIV2/SIV-Vpx 51 RSWRYWHDEQ GMSRSYTKYR YLCLMQKAVF MHFKKGCTCR GEGHGPGGWR 100

HIV1-Vpr     90 RNGASKS.... .
HIV2/SIV-Vpr 91 LSAIPPSRSM L
HIV2/SIV-Vpx 101 SGPPPPPPPG L
```

FIG. 1A

```
Vpr wt      MEQAPEDQGPQREPYNDWTLELLEELKNEAVRHFPRIWLHSLGQHIYETYGDTWTGVEALIRILQQLLFIHFRIGCRHSRIGIIQHRRTRNGASKS
E21,24P     ----------P--P----------------------------------------------------------------------------------
αL-A        ----------A-AA--A-------------------------------------------------------------------------------
A30S        ----------------S-------------------------------------------------------------------------------
A30L        ----------------L-------------------------------------------------------------------------------
A59P        ------------------------------P-----------------------------------------------------------------
L64S        ------------------------------------------S-----------------------------------------------------
L67S        ------------------------------------------------S-----------------------------------------------
L68S        ------------------------------------------------S-----------------------------------------------
H71C        ------------------------------------------------S-----------------------------------------------
H71Y        ------------------------------------------------C-----------------------------------------------
G75A        ------------------------------------------------Y-----------------------------------------------
C76S        ------------------------------------------------------A-----------------------------------------
HXB2        MEQAPEDQGPQREPYNDWTLELLEELKNEAVRHFPRIWLHSLGQHIYETYGDIWIGVEALIRILQQLLFIHFQNWVST
```

FIG.1B

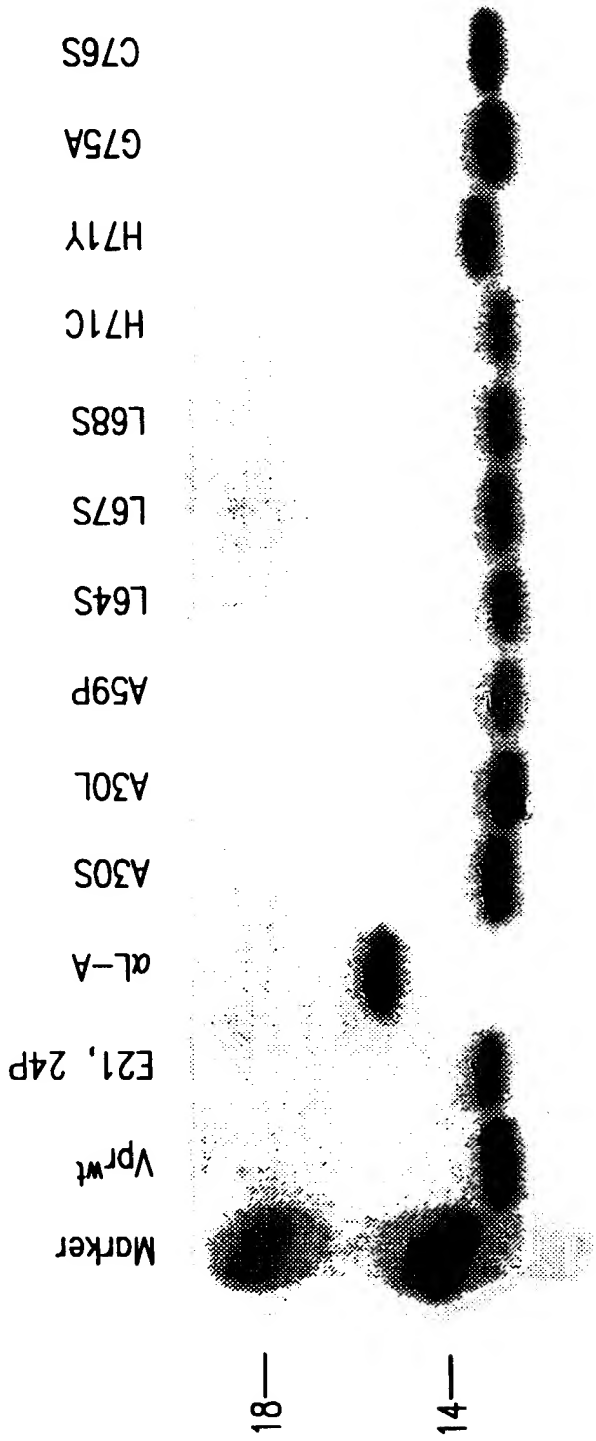
Marker
Vpr^{wt}
E21, 24P
αL–A
A30S
A30L
A59P
L64S
L67S
L68S
H71C
H71Y
G75A
C76S
14
18

FIG.1C

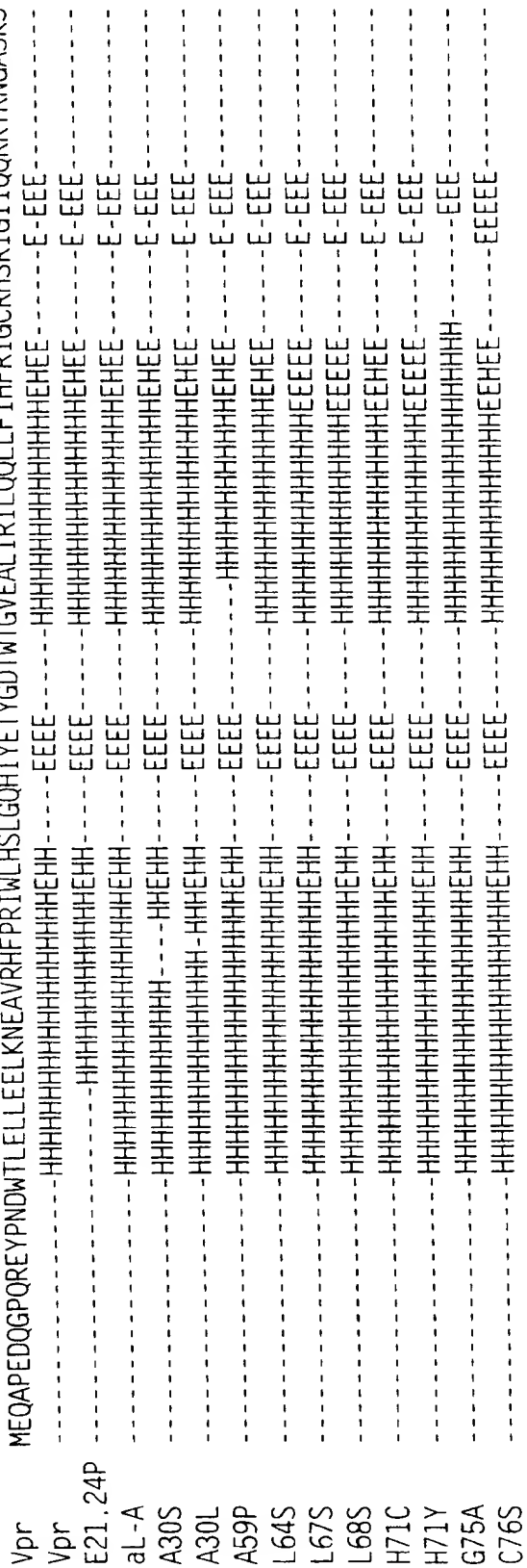
Vpr MEQAPEDQGPQREYPNDWTLELLEELKNEAVRHFPRIWLHSLGQHIYETYGDTWTGVEALIRILQQLLFIHFRIGCRHSRIGIIQQRRTRNGASKS
Vpr
E21.24P
aL-A
A30S
A30L
A59P
L64S
L67S
L68S
H71C
H71Y
G75A
C76S

FIG.1D

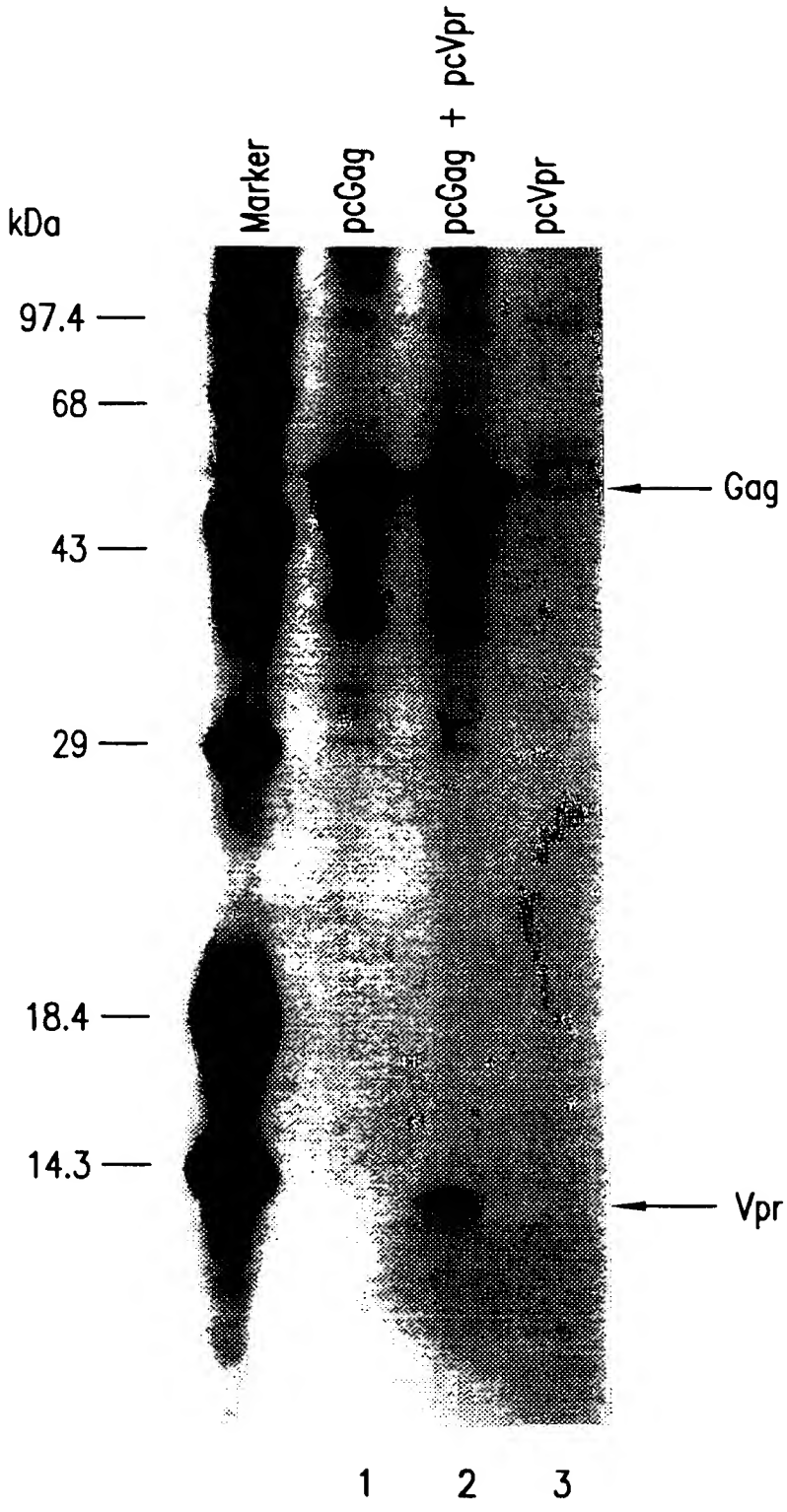
kDa
Marker
pcGag
pcGag + pcVpr
pcVpr
97.4
68
43
29
18.4
14.3
Gag
Vpr
1
2
3

FIG. 2

FIG.3A

FIG.3B

FIG.3C

FIG.3D

FIG.3E

FIG.3F

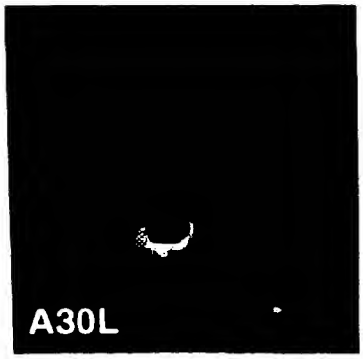

FIG.3G

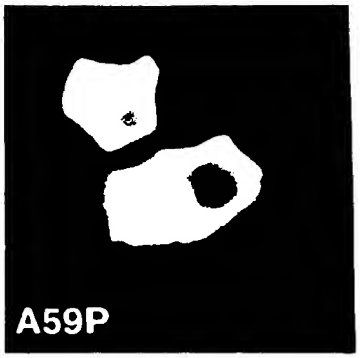

FIG.3H

FIG.3I

FIG.3J

FIG.3K

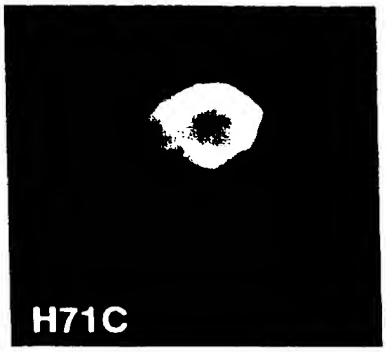

FIG.3L

FIG.3M

FIG.3N

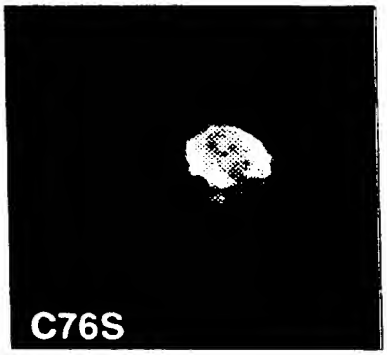

FIG.3O

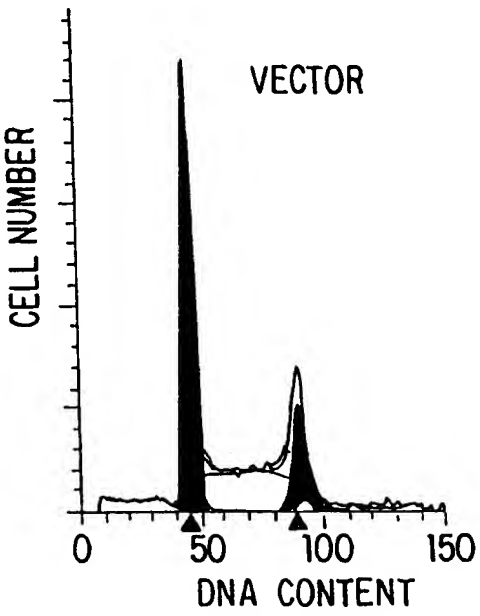

FIG. 4A-1

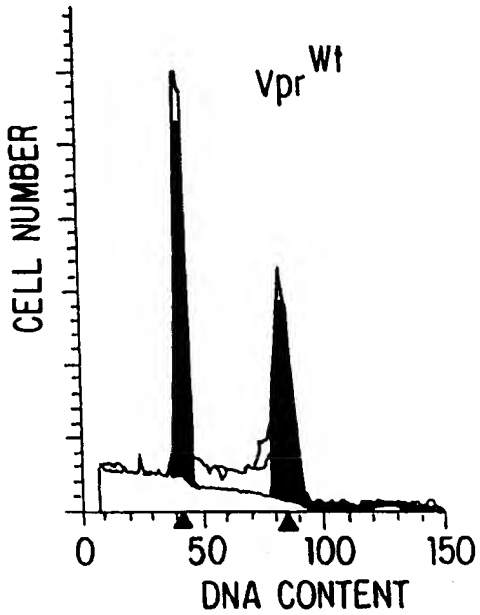

FIG. 4A-2

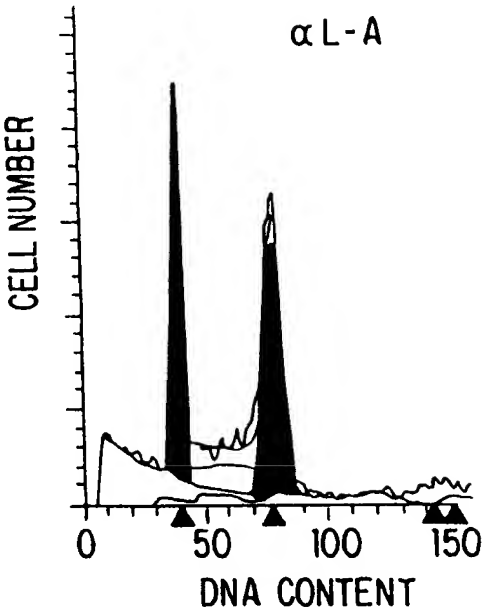

FIG. 4A-3

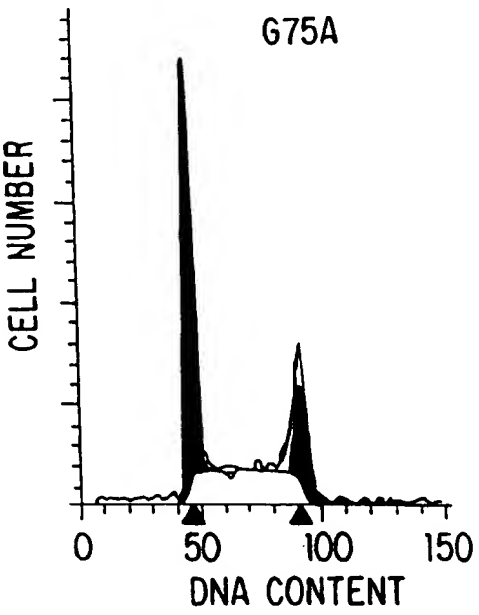

FIG. 4A-4

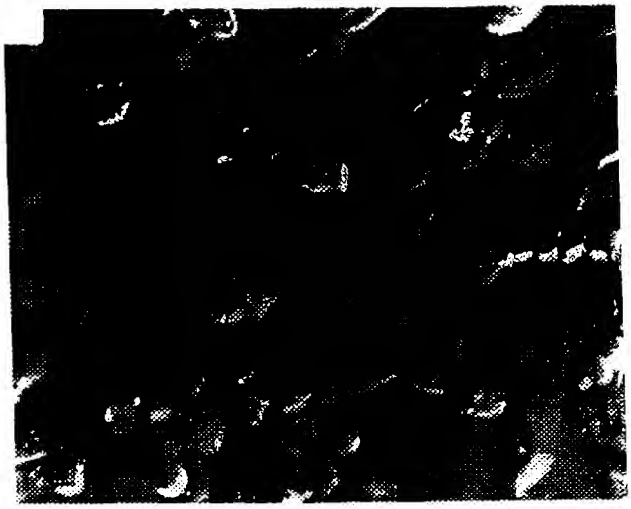

FIG.4B-1

FIG.4B-2

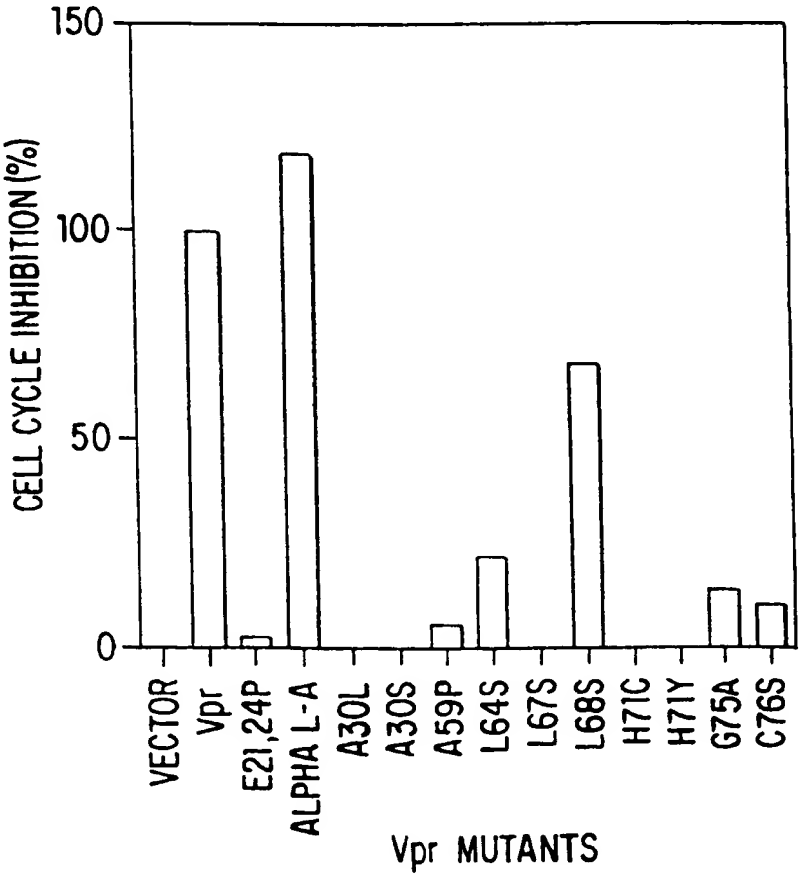
150
100
50
0
CELL CYCLE INHIBITION (%)
VECTOR
Vpr
E21,24P
ALPHA L-A
A30L
A30S
A59P
L64S
L67S
L68S
H71C
H71Y
G75A
C76S
Vpr MUTANTS

FIG. 4C

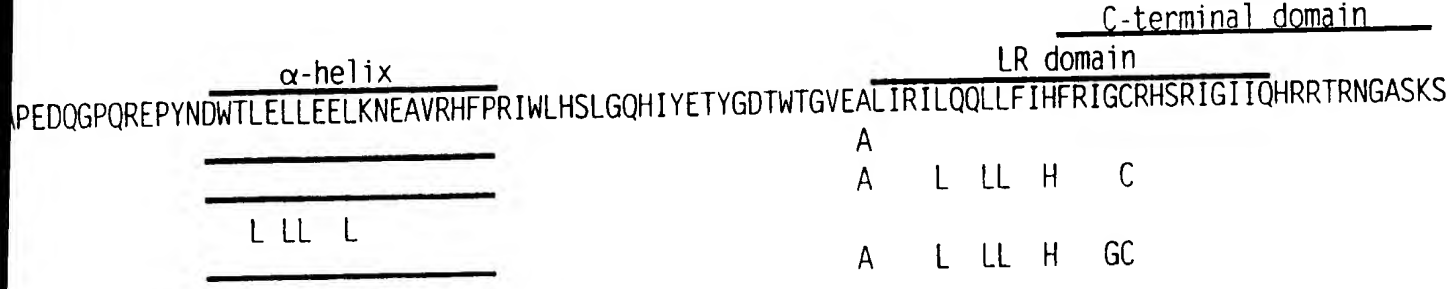

FIG.5

09/485421
PCT/US98/16890

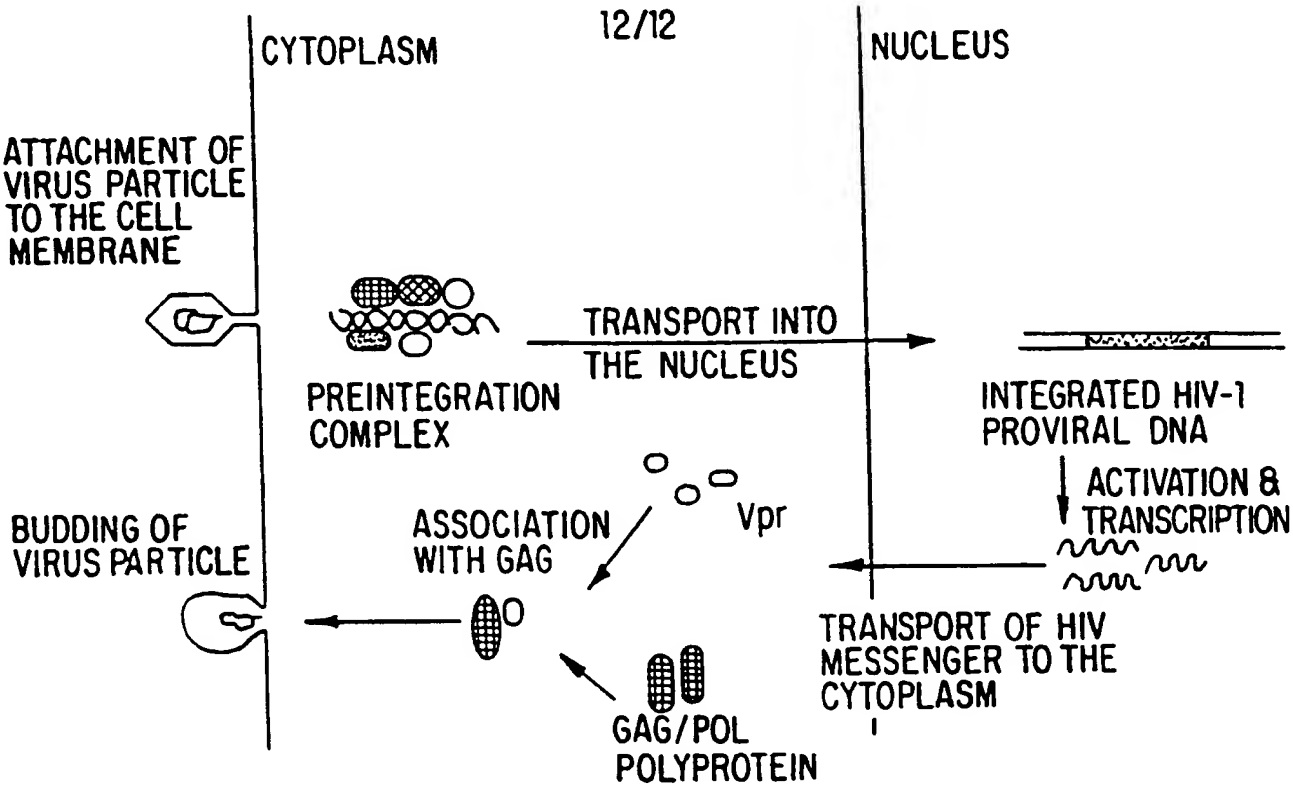
CYTOPLASM
NUCLEUS
ATTACHMENT OF VIRUS PARTICLE TO THE CELL MEMBRANE
TRANSPORT INTO THE NUCLEUS
PREINTEGRATION COMPLEX
INTEGRATED HIV-1 PROVIRAL DNA
ACTIVATION & TRANSCRIPTION
Vpr
ASSOCIATION WITH GAG
BUDDING OF VIRUS PARTICLE
TRANSPORT OF HIV MESSENGER TO THE CYTOPLASM
GAG/POL POLYPROTEIN

FIG. 6A

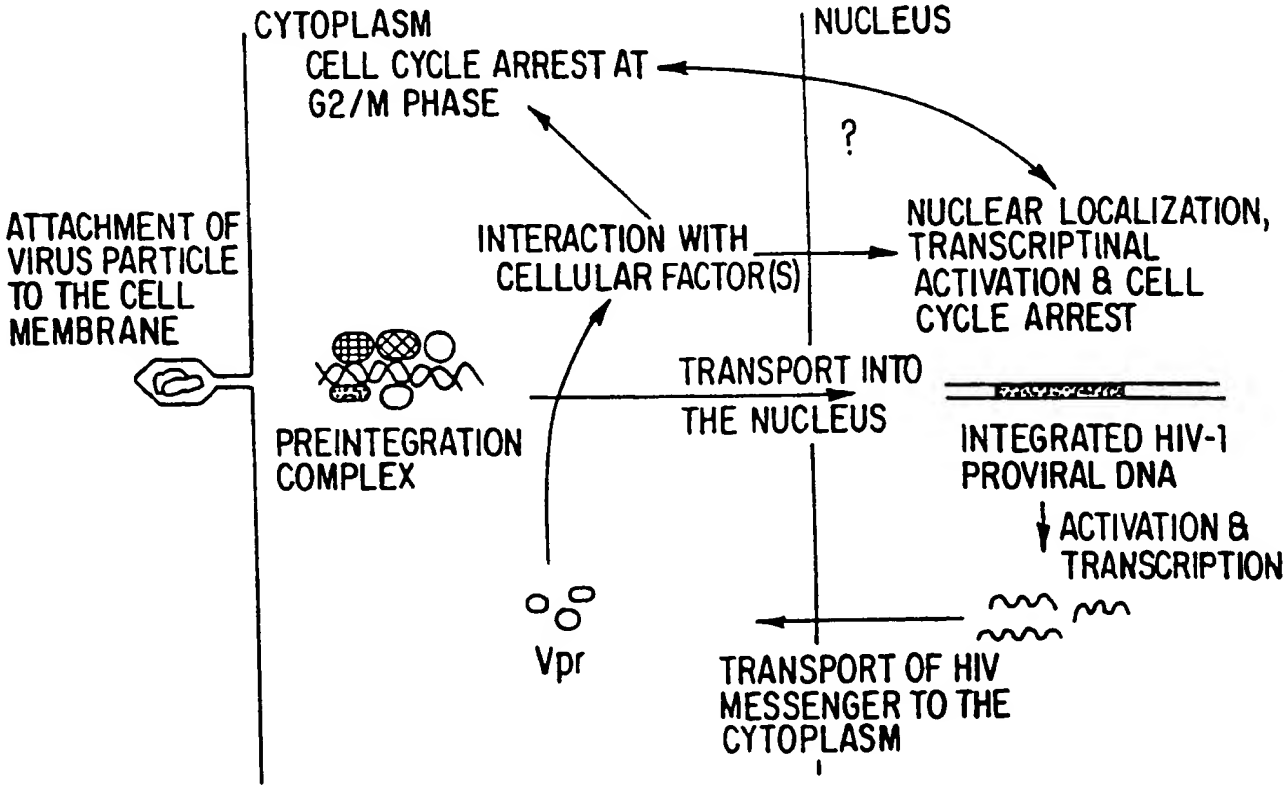
CYTOPLASM
NUCLEUS
CELL CYCLE ARREST AT G2/M PHASE
?
ATTACHMENT OF VIRUS PARTICLE TO THE CELL MEMBRANE
INTERACTION WITH CELLULAR FACTOR(S)
NUCLEAR LOCALIZATION, TRANSCRIPTINAL ACTIVATION & CELL CYCLE ARREST
TRANSPORT INTO THE NUCLEUS
PREINTEGRATION COMPLEX
INTEGRATED HIV-1 PROVIRAL DNA
ACTIVATION & TRANSCRIPTION
Vpr
TRANSPORT OF HIV MESSENGER TO THE CYTOPLASM

FIG. 6B